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LETTERS AND CORRESPONDENCE

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Complete Regression of a Suprasellar Secondary Mass in a Patient With Low-Grade Non-Hodgkin's Lymphoma (NHL) Treated With 2-Chlorodeoxyadenosine (CDA)

To the Editor: CdA penetrates into the cerebral spinal fluid (CSF) with a CSF-plasma concentration ratio of 25% [1,2]. These data are the rationale for its use in malignancies of the central nervous system (CNS) [2]. The only report on the clinical use of CdA in CNS lesions in hematologic malignancies refers to a patient with Waldenstrom's macroglobulinemia and meningeal involvement who had a complete resolution of the meningeal abnormalities [3]. We report on a 58-year-old woman with a low-grade NHL who had a secondary localization in the suprasellar region that completely regressed with CdA treatment. Lymphadenopathy in the right (rt) axillar and rt submandibular regions was noted in December 1985; diagnosis of nodular centrocytic centroblastic NHL (WFC) was made by lymph node biopsy and stage determined by standard procedures (II A-supra diaphragmatic). A complete clinical response (CCR) was obtained by radiotherapy (mantle field technique, 30 Gy with a boost dose to 46 Gy on the involved regions). In August 1989 she relapsed in the rt parotid gland and rt breast; a second CCR was achieved with 6 courses of CHOP. In March 1991, a second relapse occurred in the rt axillary lymph nodes and rt breast. Five additional courses of CHOP were given and the third CCR was obtained. In January 1995, the patient had a third relapse with extensive nodal involvement above and below the diaphragm and was treated by irradiation: pelvic (43 Gy and a boost dose to 54 Gy on bulky sites), peri-aortic (total dose 45.6 Gy), left axillary and upper jugular lymph nodes (total dose in hyperfractionated schedule on previously irradiated regions, 53.2 Gy). A new CCR was obtained. Radiotherapy was chosen because the patient had already received a total dose of Antracyclin of 500 mg/sqm with a heart ejection fraction of 38%. On April 20, 1996, the patient had fever, melena, slurry speech, and confusion. Gastroscopy evidenced several localization in the stomach and in the duodenum confirmed by biopsy. Total body CT demonstrated extensive liver, kidney, and subdiaphragmatic

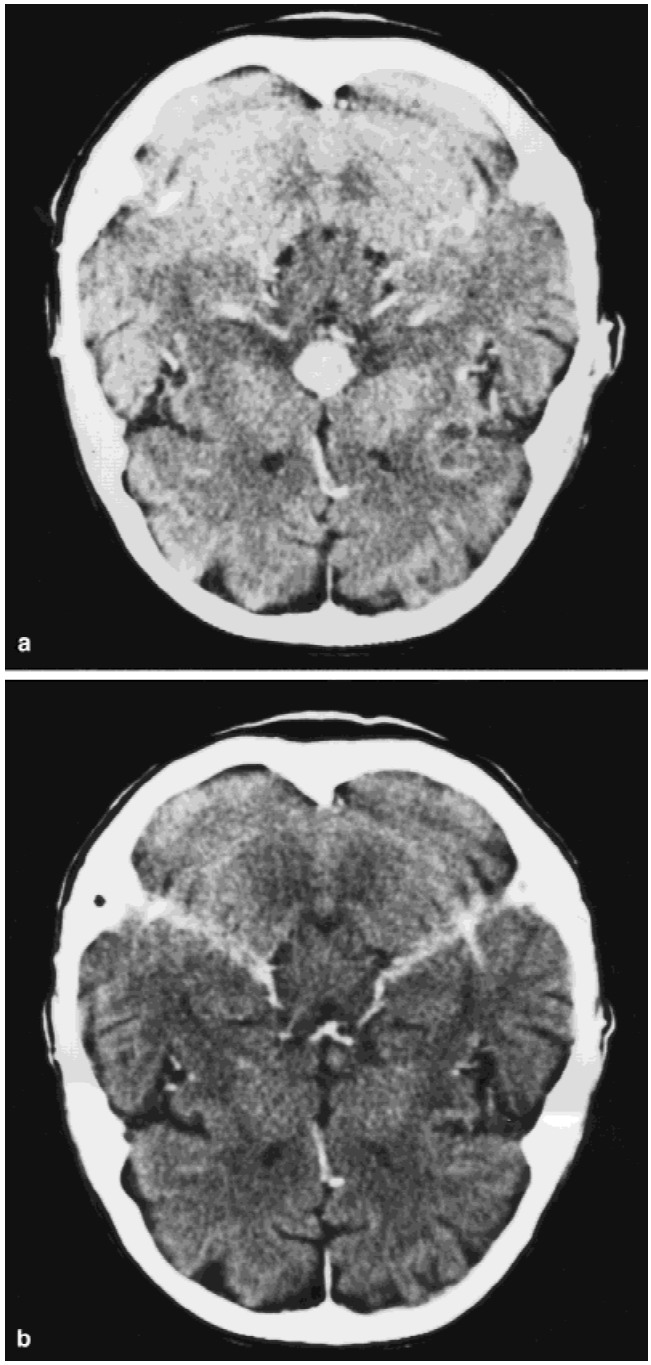

Fig. 1. a: Brain CT (May 6, 1996). Suprasellar lesion with involvement of diencephalic and chiasmatic regions and extensive peri-lesion edema. b: Brain CT after CdA therapy (May 24, 1996). Complete regression of the brain lesion.

lymph node involvement with rt ureter compression that required a stent insertion. Brain CT showed a suprasellar lesion involving the diencephalic and chiasmatic regions (Fig. 1a). The patient was treated with CdA (2 hr-infusion of 0.14 mg/kg die × 7 days) and Dexamethasone (0.3 mg/kg die × 4 days). Therapy was well tolerated without significant hematologic toxicity (WHO G4 leukopenia duration, 3 days; no thrombocytopenia). Partial regression of the liver, kidney, and lymph node involvement and complete regression of the brain lesions (Fig. 1b) were documented 1 month later by CT. The patient was discharged on May 24 with complete regression of the neurological symptoms. On June 13 she died from an acute cerebral vascular accident (CVA) of ischemic origin (brain CT not shown). In this patient, a single cycle of CdA induced complete regression of the brain lesion. CVA as a complication of therapy with CdA has not been reported; a relationship between treatment and the final event is unlikely.

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References

1. Liliemark J, Juliusson G: On pharmacokinetics of 2-chloro-2′-deoxyadenosine (CdA) in cerebrospinal fluid (CSF). Blood 80(suppl):417a (abstr. 1874), 1992.
2. Kearns CM, Blakeley RL, Santana VM, Crom WR: Pharmacokinetics of Cladribine (2-chlorodeoxyadenosine) in children with acute leukemia. Cancer Res. 54: 1235–1239, 1994.
3. Richards AL: Response of meningeal Waldenstrom's macroglobilinemia to 2-chlorodeoxyadenosine. J Clin Oncol 13:2476, 1995.

Conversion of an Acute Leukemia From a Mixed Lineage to Lymphoid Phenotype

To the Editor: Despite the fact that most of the leukemic patients at relapse exhibit the original phenotype observed at diagnosis, a lineage conversion of blast cells has been reported [1]. ''Lineage switch'' is the term that commonly defines the conversion of leukemic lineage from diagnosis to relapse. This change is usually from lymphoid to myeloid, but a change from myeloid to lymphoid phenotypic conversion has also been previously reported [2]. We herein report a rare case, probably the third, that initially presented acute mixed lineage leukemia (AMLL) and converted to lymphoid phenotype at relapse.

A 42-year-old female patient was admitted to our hospital with a 2-month history of bone pain and fatigue. Physical examination revealed pallor and slight splenic enlargement. Laboratory investigations showed erythrocyte sedimentation rate 115 mm/h, hemoglobin 10.8 g/dl, white blood cell 8,400/μl (12% blast), platelets 53,000/μl. Bone marrow smear showed 80% blasts, which were moderate in size with fine nuclear chromatin and inconspicuous nucleoli. Except for a few cells with scanty cytoplasm, most of them had a moderate amount of basophilic cytoplasm without granules and had cytoplasmic blebs with a M7-like appearance. Myeloperoxidase was positive in 6% of blasts. An immunoperoxidase staining for Factor VIII related antigen was found to be negative. Immunophenotypic analysis revealed that the blasts expressed both myeloid and lymphoid antigenic markers (Table I). Cytogenetic analysis revealed normal karyotype. Biochemical tests were within normal limits except lactic dehydrogenase (402 U/L).

She was diagnosed as AMLL and acute myeloblastic leukemia directed treatment was given. Complete remission was achieved after two cycles of treatment. Consolidation therapy could not be given because of toxic hepatitis. Four months after the induction chemotherapy, a routine complete blood count revealed relapse (10% blasts). There were 87% blasts on her bone marrow smear, which almost had the same morphologic appearance as before. Myeloperoxidase staining was negative. Immunophenotyping analysis disclosed that the blast cells had only CALLA + B cell acute lymphoblastic leukemia (ALL) antigenic characteristics (Table I). Cytogenetic studies were normal again. Complete remission was achieved by ALL directed treatment, but relapsed early. She could not receive further antileukemic treatment and died of sepsis.

TABLE I. Immunophenotyping Studies at Diagnosis and Relapse

	Diagnosis (%)	Relapse (%)
CD3	9	3
CD5	11	4
CD7	8	3
CD4	9	
CD8	4	
CD10	80	94
CD19	86	94
CD22	82	93
CD13	89	0
CD33	62	1
HLA-DR	91	95
TdT		91

As the leukemic cells exhibited both myeloid and lymphoid phenotypic features, the patient was initially diagnosed as AMLL. The overlap of the proportion of blasts positive for both B cell markers and myeloid markers suggested that they might be on the same cells [3]. Interestingly at relapse, immunophenotyping analysis demonstrated that the blasts had only lymphoid characteristics. It seems reasonable that this phenotypic conversion may be a ''lineage switch'' rather than a therapy-related secondary leukemia, because (1) cytogenetic studies that indicated normal karyotype can suggest, but not prove, the same clonal origin of blasts at diagnosis and relapse [4]; (2) ALL as a secondary leukemia has never been reported before [1].

Although the mechanism is not clear, the presence of phenotypic characteristics of more than one lineage on leukemia cells at diagnosis suggests that leukemic transformation occurs at the level of pluripotent stem cell [3,4]. A spontaneous or drug-induced capacity for transformation and differentiation of this progenitor cell may cause lineage switch [5].

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References

1. Stass S, Mirro J, Melvin S, Pui C, Murphy SB, Williams D: Lineage switch in acute leukemia. Blood 64:701, 1984.
2. Hurwitch CA, Mirro J Jr: Mixed lineage leukemia and asynchronous antigen expression. Hematol Oncol Clin North Am 4:767, 1990.
3. Stass S, Mirro J: Unexpected heterogeneity in acute leukemia: Mixed lineages and lineage switch. Human Pathol 16:811, 1985.
4. Mura R, D'Angelo P, Rizzari C, Biondi A, Giudici G, Crosti L, Castagni M, Cantu'-Rajnoldi A: Lineage switch in a childhood T-cell acute lymphoblastic leukemia. Pediatric Hematol Oncol 9:281, 1992.
5. Ben-Bassat I, Gale RP: Hybrid acute leukemia. Leuk Res 8:929, 1984.

Hypoferremia, Absent Bone Marrow Macrophage Iron, and Microcytic Anemia With Minimal Response to Iron Therapy: An Acquired Disorder of Iron Metabolism

To the Editor: We have read with great interest the report by Hartman and Barker that describes two children with an inherited disorder of iron metabolism [1]. In these patients there was intestinal iron malabsorption, but anemia was not totally corrected even with parenteral iron, suggesting a defect in the uptake of iron by erythroid bone marrow elements. We herein describe two adult patients with similar clinical features.

The first patient was a 20-year-old woman. She was admitted with a 3-month history of pallor and fatigue. The second patient was a 47-year-old man who presented with fatigue and exertional dyspnea. Both patients had normal physical examinations and there were no histories of external blood loss, chronic diarrhea, or malabsorption. Bone marrows were normocellular and macrophage iron absent. Serum vitamin B_{12} and folic acid levels were normal as were hemoglobin electrophoreses. After detailed investigations, both patients were diagnosed as ''iron deficiency anemia.'' Initial laboratory studies are presented in Table I. No cause was identified in the patients to explain iron deficiency despite an extensive work-up including radiograms of the gastrointestinal tract. Ferrous sulfate at a dose of 180 mg elemental iron was given to each patient. No reticulocyte crisis could be observed within the first week of therapy. At the end of 2 months of therapy, hemoglobin levels only slightly increased in both patients (Table I). Iron challenge studies were performed with oral ferrous sulfate. The rise in serum iron was within the expected range in both patients. Since we could not observe the desired therapeutic response with oral iron, parenteral iron dextran was administered at calculated doses to replenish diminished iron stores (1,500 mg for patient 1 and 2,000 mg for patient 2). No further increase in hemoglobin values could be noted. After oral and parenteral iron supplementation, bone marrow macrophage iron was absent by Prussian-blue staining and serum ferritin levels were low in both patients. Karyotypic analyses of the bone marrows revealed no chromosomal abnormalities.

The past medical histories of our patients were unremarkable. These patients had similar clinical features with those described by Hartman and Barker, but there were some differences. The disordered iron metabolism in our patients was acquired as judged by their previous medical records. In their patients, iron absorption was diminished, whereas in ours, iron challenge studies showed no abnormalities in the absorptive phase. In their patients, bone marrows were hypocellular; however, in our patients they were normocellular.

Regulation of iron balance is of particular interest, especially iron absorption, cellular iron metabolism, and transferrin-transferrin receptor in hematopoiesis [2,3]. Recent advances in molecular and cell biology have helped to reveal the mysteries of cellular iron metabolism concerning mRNA encoding ferritin and transferrin receptor synthesis. Although the role of transferrin in mammalian iron homeostasis has been well characterized, the study of genetic disorders of iron metabolism has revealed other, transferrin-independent, mechanisms by which cells can acquire iron [4]. The basic pathology in patients described by Hartman and Barker was a defect in the uptake of iron by erythroid bone marrow elements. On the other hand in our patients, the defect was a generalized uptake of iron by bone marrow elements including macrophages. Although iron absorption was normal, serum iron was low. We could not explain the reason for unresponsiveness to both oral and parenteral iron supplementation, but we believe that there is a complex disorder at the level of cellular iron metabolism, which awaits further clarification.

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REFERENCES

1. Hartman KR, Barker JA: Microcytic anemia with iron malabsorption: An inherited disorder of iron metabolism. Am J Hematol 51:269–275, 1996.
2. Conrad ME: Regulation of iron absorption. Prog Clin Biol Res 380:203–219, 1993.
3. Uchida T: Overview of iron metabolism. Int J Hematol 62:193–202, 1995.
4. de Silva DM, Askwith CC, Kaplan J: Molecular mechanisms of iron uptake in eukaryotes. Physiol Rev 76:31–47, 1996.

Rapid Diagnosis of Hemochromatosis Gene Cys282Tyr Mutation by SSCP Analysis

To the Editor: Hereditary hemochromatosis (HH) is perhaps the commonest disease-causing genetic disorder among Caucasians since up to 5 per 1,000 individuals are homozygous for the disease [1]. A mutation in the recently described candidate gene HLA-H has been shown to be closely associated with hemochromatosis [2]. In particular, homozygosity for the nucleotide substitution 845G → A (Cys282Tyr) accounts for the vast ma-

TABLE I. Laboratory Results of the Patients at Initial Presentation and at Second Month of Therapy*

	Before therapy with oral iron		After therapy with oral iron		
	Patient 1	Patient 2	Patient 1	Patient 2	Normal range
Hemoglobin	7.3	7.8	8.1	8.4	Male: 14–18 g/dl Female: 12–16 g/dl
MCV	64	68	67	71	80–100 fl
MCHC	23	24	24	25	31–36 g/dl
Ferritin	1	3	2	4	Male: 20–250 μg/L Female: 10–120 μg/L
Serum iron	13	18	15	20	Male: 65–175 μg/dl Female: 50–170 μg/dl
Serum TIBC	485	462	467	455	250–450 g/dl
% TS	2.7	3.9	3.2	4.2	>15%

*MCV: mean corpuscular volume; MCHC: mean corpuscular hemoglobin concentration; TIBC: total iron binding capacity; TS: transferrin saturation.

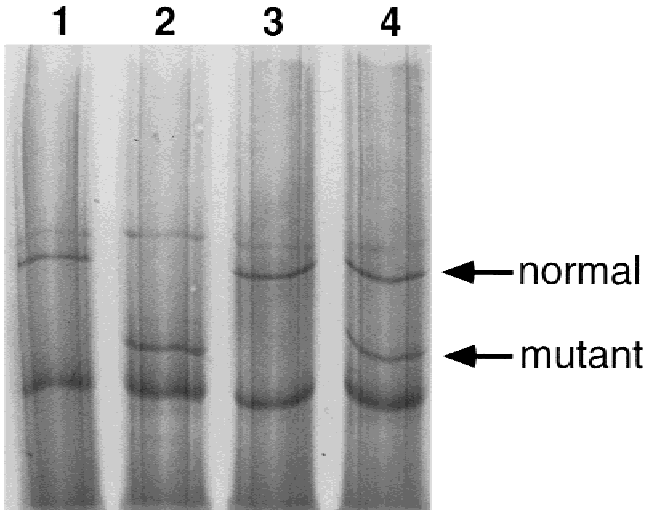

Fig. 1. SSCP analysis readily distinguishes normal, heterozygotes, and homozygotes for the 845G→A mutation in HH. Lanes 1, normal; 2, homozygous; 3, normal; 4, heterozygous.

jority (83–100%) of affected individuals [2,3]. Detection of this mutation relies upon DNA extraction, enzymatic amplification of DNA by PCR, and subsequent restriction enzyme digestion and gel electrophoresis of digested fragments. However, this method can be associated with difficulties in genotype assignment because of incomplete restriction enzyme digestion of amplified products. Additionally, the time and expense involved in formal DNA extraction and restriction enzyme digestion militates somewhat against its application on a wider, population-based scale.

We have designed a detection method in which blood is simply boiled, the released DNA amplified by PCR, and then subjected to analysis by single-strand conformational polymorphism (SSCP). SSCP analysis allows the detection of single base changes in DNA fragments due to mobility differences of single-stranded DNA under non-denaturing conditions [4]. Specifically, 50 μl of whole blood are diluted in 50 μl of water, heated to 100°C for 15 min, centrifuged, and aliquots of 2 μl taken for PCR. DNA amplification is performed using primers previously described [2] and thermal cycles of 94°C for 10 sec, 60°C for 10 sec, and 72°C for 10 sec, for a total of 35 cycles. Subsequently, samples are heated for 5 min at 96°C in formamide-containing gel loading buffer and placed on ice. Finally, 2-μl aliquots are subjected to electrophoresis on a 7.5% polyacrylamide gel using the Phast™ gel system (Pharmacia, Piscataway, NJ) prior to staining with silver nitrate. In all cases, genotype determination by SSCP was shown to be identical with that derived from restriction enzyme digestion of amplified DNA using *Rsa*I, as described elsewhere [5].

In the gel shown (Fig. 1), the mutant allele is readily distinguishable from the normal allele, which allows assignment of both homozygous and heterozygous states, without the need for prior restriction enzyme digestion.

This form of genetic analysis offers considerable advantages in relation to time, expense, and reproducibility. By boiling diluted blood, DNA extraction with proteinase K and phenol/chloroform is obviated. Furthermore, potential problems encountered with partial restriction enzyme digestion are circumvented. Moreover, SSCP analysis of the common hemochromatosis genetic defect permits rapid screening of family members of affected individuals as well as larger, population-based studies.

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References

1. Edwards CQ, Griffin LM, Goldgar D, Drummond C, Skolnick MH, Kushner JP: Prevalence of hemochromatosis among 11,065 presumably healthy blood donors. N Engl J Med 318:1355–1362, 1988.
2. Feder JN, Gnirke A, Thomas W, Tsuchihashi Z, Ruddy DA, Dormishian F, Domingo R Jr, Ellis MC, et al: A novel MHC class I-like gene is mutated in patients with hereditary haemochromatosis. Nat Genet 13:399–408, 1996.
3. Jazwinska EC, Cullen LM, Busfield F, Pyper WR, Webb SI, Powell LW, Morris PC, Walsh TP: Haemochromatosis and HLA-H. Nat Genet 14:249–251, 1996.
4. Orita M, Iwahana H, Kanazawa H, Hayashi K, Sekiya T: Detection of polymorphisms of human DNA by gel electrophoresis as single-strand conformation polymorphisms. Proc Natl Acad Sci USA 86:2766–2770, 1989.
5. Chang J-G, Liu T-C, Lin S-F: Rapid diagnosis of the HLA-H gene Cys282Tyr mutation in haemochromatosis by polymerase chain reaction: A very rare mutation in the Chinese population. Blood 89:3492–3493, 1997.

Sphingosine-Phosphate Content in the Plasma of Platelet Concentrates Correlates With Poor Platelet Increments After Transfusion and With Occurrences of Transfusion Reactions in Patients

To the Editor: Recent studies suggest that complications after platelet transfusion are often caused by bioactive substances formed in the platelet concentrates during storage. Likely candidates considered for causing detrimental reactions have been cytokines such as IL-1β, IL-6, or TNFα, released from contaminating leukocytes during storage [1] although other studies do not completely support this theory. We found that sphingosine1-phosphate (Sph-1-P), a novel bioactive sphingolipid, is abundantly stored in platelets and released extracellularly upon stimulation, and acts as an autocrine stimulator of platelets [2]. Recently, a very small amount of Sph-1-P (nM order) was reported to affect atrial myocyte acetylcholine-sensitive K^+ channel, which is considered to be related to pacemaker roles of heart function [3]. This may be related to our finding that Sph-1-P injection in mice (i.v., 10 mg/kg mouse) caused immediate rigors and death. Other studies reported that, together with sphingosine, it plays mediatory roles in the immediate negative inotropic effects of TNFα on cardiac myocytes, and that it induces rapid neurite retraction in cultured neuronal cells. We recently established a new, facile method to quantify Sph-1-P, utilizing N-acetylation of Sph-1-p with radioactive acetic anhydride [4]. Using this method, we found that Sph-1-P is a normal constituent of human plasma and serum. These observations from our laboratory and others strongly suggest pathophysiological roles of the Sph-1-P released from platelets into the blood vessels.

In this study, to examine the relationships between plasma Sph-1-P contents in platelet concentrates and occurrences of complications as well as corrected count increments (C.C.I.) after transfusion, we measured Sph-1-P contents in the plasma from platelet samples given for transfusions to patients (Johns Hopkins Hospital, Baltimore) with or without subsequent transfusion reactions (fever, vomiting, etc.) and with differing C.C.I. values. We have obtained two important findings (Fig. 1): (1) Poor platelet C.C.I. after transfusion correlates strongly with high Sph-1-P content in transfused platelet plasma; (2) A striking difference in Sph-1-P content between the non-reaction and the transfusion reaction groups is apparent, namely 0.71 ± 0.19 nmol/600 μl plasma ($n = 50$) and 1.1 ± 0.28 nmol/600 μl plasma ($n = 36$), respectively (P value of Students t-test < 0.001). We have also observed a 2–3-fold increase of Sph-1-P in plasma during 5 days storage. Aged platelet concentrates are often claimed to cause more complications and poor C.C.I. These results together strongly suggest that Sph-1-P released from stored platelets is another possible candidate substance, besides various cytokines, causing platelet transfusion reactions and

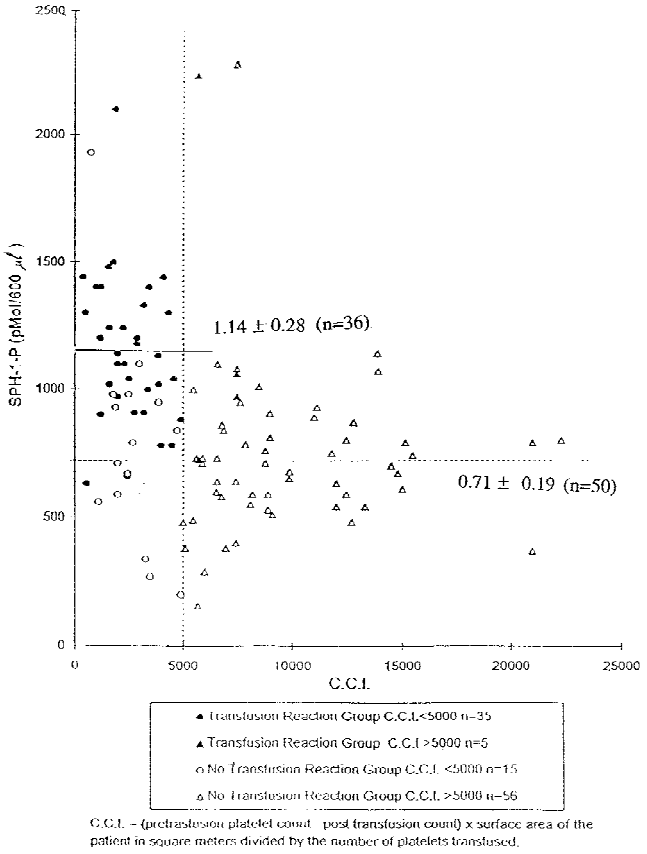

Fig. 1. Sphingosine 1-phosphate content in platelet plasma samples correlates with poor platelet increments after transfusion and occurrences of transfusion reactions in patients.

poor C.C.I. in the patients . They also imply that inhibitors of Sph-1-P synthesis in or release from activated platelets, such as methylsphingosines [5], would be possible candidates for efficient drugs to mitigate platelet transfusion reactions and to improve poor C.C.I. after transfusion.

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REFERENCES

1. Stack G, Snyder EL: Cytokine generation in stored platelet concentrates. Transfusion 34:20, 1994.
2. Yatomi Y, Ruan F, Hakomori S, Igarashi Y: Sphingosine 1-phosphate: A platelet-activating sphingolipid released from antagonist-stimulated human platelets. Blood 86:193, 1995.
3. Bunemann M, Brandts B, zu Heringdorf DM, van Koppen CJ, Jakobs KH, Pott L: Activation of muscarinic K^+ current in guinea-pig atrial myocytes by spingosine 1-phosphate. J. Physiol (Lond) 489:701, 1995.
4. Yatomi Y., Ruan F, Ohta H, Welch RJ, Hakomori S, Igarashi Y: Quantitative measurement of sphingosine-1-phosphate in biological samples by acylation with radioactive acetic anhydride. Anal. Biochem. 230:315, 1995.
5. Yatomi Y, Ruan F, Megidish T, Toyokuni T, Hakomori S, Igarashi Y: *N,N*-dimethylsphingosine is a potent inhibitor of sphingosine kinase and regulates sphingosine 1-phosphate activity in human platelets. Biochemistry 35:626, 1996.

Schwachman or Pearson Syndrome

To the Editor: I have read with enthusiasm Oksel and Tanelli's interesting short case report in the January issue of the journal (54; 84, 1997). In addition to malabsorption and marked growth retardation, this 7-year-old boy had other findings affecting different systems such as hematologic (neutropenia), immunologic (hypogammaglobulinemia, low T-helper cells, and reversed T4/T8 ratio), and bone (infantile vertebrae, acetabular hypoplasia, right femur neck shortness). In spite of marked hypogammaglobulinemia (IgG: 107 mg/dl, IgM: 17 mg/dl) and cyclic neutropenia, no history of severe infections was mentioned.

This young boy's findings were not very compatible with Schwachman-Diamond syndrome [2] in which anemia is accompanied by pancreatic insufficiency without lung involvement and normal sweat electrolytes as in Oksel and Tanelli's case. However, other systems are usually not involved in Schwachman-Diamond syndrome. But, in Pearson syndrome, which is a mitochondrial disorder, neutropenia including vacuolisation of erythroid and myeloid precursors and involvement of other systems occurs, as in Oksel and Tanelli's case.

I do not think that the syndrome of exocrine pancreatic insufficiency with congenital anomalies should be considered in that case because of hematological findings that have not to my knowledge been described in that syndrome [3].

The diagnosis of Pearson syndrome could easily be ruled out in Oksel and Tanelli's case by mitochondrial DNA studies [4].

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REFERENCES

1. Pearson HA, Lobel JS, Kocvshis SA, et al: A new syndrome of refractory sideroblastic anemia with vaculization of marrow precursors and exocrine pancreatic dysfunction. J Pediatr 95:976–984, 1979.
2. Cormier V, Rötig A, Rasore A, et al: Widespread multi-tissue deletions of mitochondrial genome in the Pearson marrow-pancreas syndrome. J Pediatr 117:599–602, 1990.
3. Schussherni A, Choi SJ, Silverberg M: Exocrine pancreatic insufficiency with congenital anomalies. J Pediatr 89:782, 1976.
4. Aytemiz Gürgey A, Rötig A, Gümrük F, et al: Pearson's marrow pancreas syndrome in two Turkish Children. Acta Haematol 87:206–920, 1992.

Platelet Function and Simultaneous Thrombelastograms From Whole Blood and Plasma

To the Editor: Thrombelastagraphy is a global hemostaseologic investigation that is performed using whole blood. The maximal amplitude (MA) of the thrombelastographic recording represents a measure of the absolute

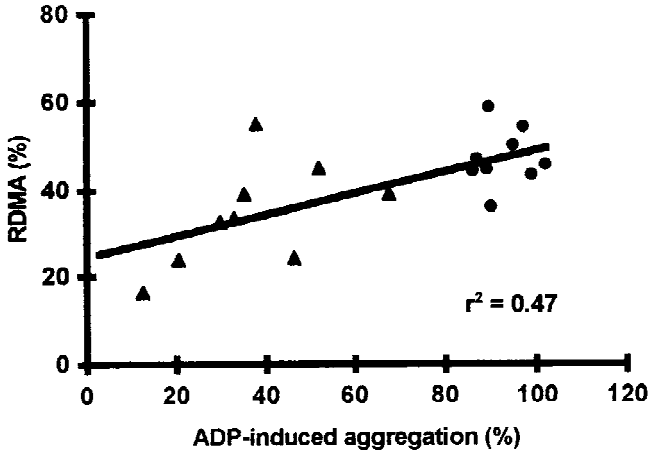

Fig. 1. Correlation between the maximal amplitude of the ADP-induced platelet aggregation tracings and the relative difference in maximal amplitude (RDMA) of thrombelastographic tracings from whole blood and plasma after incubation of samples from 9 blood donors (n = 18) with trapidil (triangles) and with phosphate buffered saline (circles).

strength of the fibrin clot and is determined by the fibrinogen concentration, by factor XIII activity, and by the platelet function and platelet count [1]. Because each of these factors can cause a reduced MA of the tracing, thrombelastography has limited usefulness in the diagnosis of platelet dysfunction. We performed thrombelastograms simultaneously from citrated whole blood and plasma to test whether the relative MA decrease of the thrombelastogram from plasma (in which platelets do not contribute to clot strength) can yield information about the platelet function.

Blood from 32 subjects was drawn into citrate tubes. Platelet count was determined and platelet aggregation studies were performed with ADP and collagen at final concentrations of 10 mM and 10 μg/ml, respectively. Thrombelastograms from citrated blood and plasma were recorded simultaneously with a 2-channel thrombelastograph (Hellige, Freiburg, Germany). Correlation between the maximum amplitudes of the platelet aggregation tracings, platelet number, and the relative difference in MA (RDMA) of the 2 thrombelastographic tracings (RDMA = [(MA whole blood tracing − MA plasma tracing)/(MA whole blood tracing)] × 100) were assessed. In 9 additional subjects, blood samples were incubated for 15 min with trapidil (a platelet aggregation inhibitor [2]) to a final concentration of 300 μg/ml and with phosphate buffered saline (control samples).

Significant correlations were found between RDMA and the maximal amplitude of the platelet aggregation tracings (correlation coefficient $r = 0.5922$, $P = 0.0004$; and $r = 0.3739$, $P = 0.035$ for collagen- and ADP-induced aggregation, respectively). The correlation between RDMA and platelet count did not attain significance ($r = 0.323$, $P = 0.0714$).

The maximal amplitudes of the ADP- and collagen-induced platelet aggregation tracings from the samples treated with trapidil were significantly decreased compared to controls (37.13 ± 16.5% vs. 92.92 ± 5.6%, $P < 0.0001$; and 23.71 ± 8.5% vs. 91.07 ± 5%, $P < 0.0001$, respectively). The RDMA of the whole blood and plasma thrombelastographic tracings from trapidil-treated samples was also significantly decreased when compared to controls (34.24 ± 11.7% vs. 46.84 ± 6.7%, $P = 0.0073$). When trapidil-treated samples and controls were analysed together ($n = 18$), there was a significant correlation between the RDMA and the maximal amplitude of the collagen- and ADP-induced (Fig. 1) platelet aggregation tracings ($r = 0.5291$, $P = 0.024$ and $r = 0.6858$, $P = 0.0017$, respectively).

We found a significant correlation between the RDMA of the simultaneously performed whole blood and plasma thrombelastograms and the platelet function as assessed by platelet aggregation. Correlations between whole blood thrombelastography parameters and plasmatic coagulation tests or platelet count and aggregation response have also been described by others [3,4]. In our study, the correlation of the RDMA with the platelet count did not attain statistical significance. This confirms previous reports, which indicate that the platelet function rather than the platelet count is the determinant of clot stability [5]. The significant correlation of the RDMA with platelet aggregation tracings from normal subjects and the fact that the correlation was preserved even though the RDMA decreased significantly when platelet function was inhibited, indicates that the RDMA from simultaneous whole blood and plasma thrombelastograms could be used to detect platelet dysfunction.

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References

1. Mallet SV, Cox DJA: Thrombelastography. Br J Anaesthesia 69:307–313, 1992.
2. Mest HJ: Trapidil: A potent inhibitor of platelet aggregation. J Drug Dev 3:143–149, 1990.
3. Zuckerman L, Cohen E, Vagher JP, Woodward E, Caprini JA: Comparison of thrombelastography with common coagulation tests. Thromb Haemost 46:752–756, 1981.
4. Tuman KJ, McCarthy RJ, Patel RV, Patel RB, Ivankovich A: Comparison of thrombelastography and platelet aggregometry. Anesthesiology 75:A433, 1991.
5. Glover CJ, McIntire LV, Brown CH, Natelson EA: Dynamic coagulation studies. Influence of normal and abnormal platelets on clot structure. Thromb Res 7:185–198, 1975.

Pseudotumor of Calcaneus: Treatment With Radiotherapy and Replacement Therapy

To the Editor: Pseudotumor is a rare and serious complication of hemophilia occurring in <1% of patients with factor VIII and IX deficiency. It is commonly seen in the long bones of the extremities and the pelvis [1]. Pseudotumor of the calcaneus is rare and difficult to manage [2]. We report a case of calcaneus pseudotumor successfully treated with radiotherapy and factor replacement.

A 15-year-old boy with moderate hemophilia A (FVIII 2.9% of normal pooled plasma) presented with a progressively increasing painful swelling of the left heel for 1 year. He was unable to bear weight and walk without support for the last 6 months. Examination revealed a swelling of the left heel measuring 10 cm in diameter. The movements at the ankle and subtalar joints were restricted. Skiagram showed an expansile lesion of the calcaneus suggestive of pseudotumor (Fig. 1). To prevent limb shortening and the need for a weight-bearing prosthesis following surgical excision of

Fig. 1. Radiograph of left foot showing pseudotumor of the calcaneus. There is an expansile lesion, thinning of the cortex, and destruction of trabecular pattern.

Fig. 2. Radiograph of calcaneus taken 3 months after treatment shows healing of the pseudotumor with secondary calcification.

the pseudotumor, the patient was treated conservatively with radiotherapy (1,400 cGY over 10 days) and factor VIII replacement (to maintain the factor level between 20–30% of normal for 6 weeks). Clinical improvement occurred within a week of treatment with relief of pain and decrease in the size of swelling. The radiograph after 3 months of therapy showed healing of the pseudotumor (Fig. 2). The patient was able to bear weight by 1 month and walk without support by 3 months.

Radiotherapy either alone or in combination with factor replacement has shown promising results in the treatment of hemophilic pseudotumors. It has been proposed that irradiation damages the fine blood vessels supplying the pseudotumor, resulting in fibrosis and healing [3]. There is prompt relief of pain and decrease in soft tissue swelling. Secondary calcification of the pseudotumor occurs within 4 weeks of therapy and complete healing by 8–12 weeks. Castaneda et al. [4] have reviewed 14 patients with 17 pseudotumors treated with radiation either alone or in combination with factor replacement. The radiation dose varied between 750–2,350 cGY. Fourteen of these 17 pseudotumors showed complete resolution. Three patients with factor VIII inhibitors also responded to radiotherapy and factor IX replacement therapy.

Krill and Mauer [2] reviewed 8 cases including 1 patient reported by Chen [5] for treatment and outcome. Five patients had received only replacement therapy (plasma or factor concentrates), one patient each underwent amputation and immobilization, respectively. Patients on conservative therapy required prolonged treatment for improvement. The patient who underwent amputation had prolonged postoperative hemorrhage and could walk only after 2 years with a prosthesis. The patient treated by Chen with radiotherapy alone had rapid resolution of pseudotumor without any recurrence for over 7 years [5]. Based upon our experience and review of literature, it is suggested that radiotherapy with replacement therapy should be preferred for treating pseudotumors of the small bones of hand and feet.

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References

1. Gillbert MS: Hemophilic pseudotumor. In Brenkhous KM, Hemuker HC (eds): ''Handbook of Hemophilia.'' New York: Elsevier, 1975, p 435.
2. Krill CE, Mauer AM: Pseudotumors of calcaneus in christmas disease. J Pediatr 77:848, 1970.
3. Reinhold HS: Structural changes in blood vessels. Curr Top Radiat Res Q 10:58, 1974.
4. Castaneda VL, Parmley RT, Bozzini M, Feldmeir JJ: Radiotherapy of pseudotumors of bone in hemophiliacs with circulating inhibitors to factor VIII. Am J Hematol 36:55, 1991.
5. Chen YF: Bilateral hemophilic pseudotumors of the calcaneus and cuboid treated by irradiation. J Bone J Surg 47A:517, 1965.

Hyperammonemic Encephalopathy in Multiple Myeloma

To the Editor: Hyperammonemia can cause an acute confusional state in patients with multiple myeloma. We present a case of hyperammonemia as a cause of delirium in a patient with multiple myeloma and normal liver function.

A 70-year-old white male presented after falling due to weakness and dizziness. He complained of nausea and 2 months of left-sided rib pain. Past medical history was significant for anemia of unknown etiology. Medications were aspirin, verapamil, doxazosin, and ibuprofen. The physical exam revealed the patient was alert, oriented, afebrile, orthostatic, and tachycardic. Crackles were present over the right lung base. Neurologic exam was unremarkable. Laboratory evaluation revealed: leukocyte count 4.7 K/μL, hematocrit 34 ml/dL, MCV 90 fl/rbc, sodium 134 mmol/dL, chloride 94 mmol/L, BUN 23 mg/dL, creatinine 2.7 mg/dL, uric acid 10.9 mg/dL, total serum protein 10.0 g/dL, albumin 3.3 g/dL, calcium 15.2 mg/dL. The skeletal survey showed multiple lytic lesions. Serum immunoglobins revealed an IgG of 4,520 mg/dL. Serum electrophoresis showed a gamma level of 3.76 g/dL. B2 microglobulin was 5.78 mg/dL. The patient was successfully treated for hypercalcemia. Subsequently he became confused. Neurologic exam was nonfocal; computed tomography of the brain was unremarkable. Repeat leukocyte count, chest radiograph, blood and urine cultures were unremarkable. Coarse upper extremity jerk-

ing and asterixis were noted. Serum ammonia level was 86 μmol/L (0–40). Additional laboratory data showed: GGT 21 U/L, AST 86 U/L, ALT 42 U/L, LDH 253 U/L, PTT 27.3 sec, INR 1.1, calcium 9.8 mg/dL, and creatinine 2.3 mg/dL. Repeated ammonia level was 96 μmol/L. Glycine to tyrosine ratio was elevated at 8. Lactulose enemas were initiated. The patient developed increasing confusion, subsequent obtundation, and expired due to respiratory failure.

In patients with multiple myeloma several causes are routinely considered for confusional states. Hypercalcemia was not felt to be the etiology in this patient as calcium was decreasing while his mental status worsened. Renal failure was excluded, and no infection was identified. Hyperviscosity syndrome was not felt to be likely as the IgG level was less than 6 g/dL. The cause of encephalopathy appeared to be hyperammonemia. There have only been 8 other patients with idiopathic hyperammonemia and advanced multiple myeloma reported in the literature [1–3]. Matsuzaki et al. compared patients with hyperammonia associated with multiple myeloma (stage III) and patients with hyperammonemia due to liver failure. It was determined that the two groups had different amino acid disturbances. The patients with multiple myeloma had elevated glycine and aspartic acid levels, and normal to decreased levels of the other amino acids [1].

Diagnosis should involve exclusion of the well-known causes of confusion in multiple myeloma. Serum ammonia level should be part of the laboratory evaluation. If abnormal, additional tests should include serum amino acids and liver function tests [4]. Therapy is another area that needs further research. It appears that the best approach is prompt chemotherapy for the underlying multiple myeloma. Therapy aimed at temporarily decreasing ammonia levels, such as lactulose and neomycin, should be considered [4]. Other possible therapies include hemodialysis, protein restriction, intubation, and controlled ventilation [4,5].

Hyperammonemia is an important cause of acute confusional state in multiple myeloma. Due to lack of knowledge about this process, central nervous system changes may be attributed to one of the more well-known causes. As this process tends to be rapidly progressive, an ammonia level should be obtained early in confused multiple myeloma patients.

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References

1. Matsuzaki H, Hata H, Sonoki T, Matsuno F, Kuribayashi N, Yoshida M, Nagasaki A, Murata H, Fujiyama S, Takatsuki K: Serum amino acid disturbance in multiple myeloma with hyperammonemia. Int J Hematol 61:131–137, 1995.
2. Caminal L, Castellanos E, Mateos V, Astudillo A, Moreno C, Dieguez MA: Case report: Hyperammonemic encephalopathy as the presenting feature of IgD multiple myeloma. J Intern Med 233:277–279, 1991.
3. Fine P, Adler K, Gerstenfeld D: Idiopathic hyperammonemia after high-dose chemotherapy. Am J Med 86:629, 1989.
4. Flanner DB, Hsai YE, Wolf B: Current status of hyperammonemic syndromes. Hepatology 2:495–506, 1992.
5. Mitchell BR, Wagner J, Karp J, Watsun AJ, Saul MB, Brusilow W: Syndrome of idiopathic hyperammonemia after high-dose chemotherapy: Review of nine cases. Am J Med 85:662–667, 1988.

Lack of Prognostic Significance of CD34 Expression in Adult AML When FAB M0 and M3 Are Excluded

To the Editor: We read with interest the paper by Fruchart et al. [1] reporting the relationship between CD34 expression and chromosomal abnormalities but not clinical outcome in acute myelogenous leukemia. Numerous studies have been performed to identify prognostic markers in patients with adult acute myelogenous leukemia (AML). The expression of CD34 antigen on blast cells in AML has been regarded as a poor prognostic factor [2–4]. However, recent clinical reports on this issue are still controversial [1,5]. We evaluated the relationship between CD34 expression and several prognostic factors: FAB classification, WBC counts, chromosomal abnormalities, and Auer bodies. Ninety-three adult patients with AML newly diagnosed in the past 5 years were studied. FAB classification of 93 patients was as follows: M0 13, M1 10, M2 36, M3 11, M4 15, M5 5, M6 4. The case with myelodysplasia was excluded. Immunophenotyping was performed for all cases. The relationship between CD34 expression and clinical outcome was evaluated in 37 cases. Thirty-seven patients were treated according to the Japan Adult Leukemia Study Group's (JALSG) protocol for AML, using behenoyl cytosine arabinoside, daunorubicin, 6-mercaptopurine with or without etoposide, and 8 patients with FAB M3 who received all trans retinoic acid as induction therapy. Thirty-four cases were classified as follows: M0 2, M1 4, M2 13, M3 8, M4 4, M5 2, M6 1. A positive reaction of CD34 was defined as >20% of leukemic cells. Fifty-seven of the 93 cases (61%) were CD34 positive. Thirteen (100%) of FAB M0 cases were CD34 positive and 10 (91%) of FAB M3 cases were CD34 negative. There were no differences in other FAB types. No correlation was seen between CD34 and WBC counts or Auer bodies. But CD34 positive cases showed a significantly higher number (59%) of chromosomal abnormalities ($P = 0.01$). Eighteen of the 37 (49%) patients treated with the same protocol were CD34 positive. The complete remission rates of CD34 positive and negative were 72% (13/18) and 95% (18/19) ($p = 0.06$). Overall survival of CD34 positive and negative patients at 3 years was 32 and 61%, respectively. The prognosis of CD34 negative patients was significantly better than that of CD34 positive patients ($P < 0.05$). It is known that the prognosis of FAB M3 is significantly better than other types of AML, and FAB M0 has a poor prognosis. Overall survival was reevaluated in 27 patients without FAB M0 and M3, because 2 (100%) of FAB M0 cases were CD34 positive and 8 (100%) of FAB M3 cases were CD34 negative. Overall survival of CD34 positive and negative patients who were not FAB M0 or M3 at 3 years was 43 and 42%, respectively (Fig. 1). No significant difference was seen between the two groups. FAB M0 and M3 should be excluded in this study, because most FAB M0 patients who had a poor prognosis were CD34 positive and most FAB M3 patients who had a good prognosis were CD34 negative. In most past studies, FAB M0 and M3 cases were not excluded from the evaluation of the relationship between CD34 expression and clinical outcome [1–4]. But Ciolli et al. [5] excluded FAB M3 patients and they could not confirm the prognostic relevance of CD34.

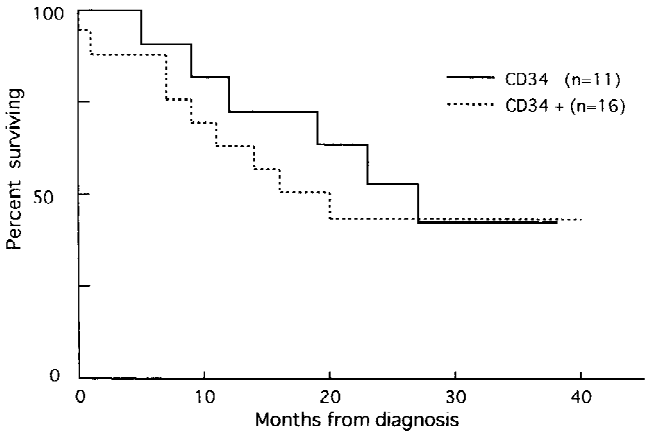

Fig. 1. Kaplan-Meier estimate of overall survival in CD34 positive and negative patients with AML (n = 27). No significant difference was seen between the two groups.

Our study was too small to discuss the relationship between CD34 expression and clinical outcome. We conclude that large studies involving patients without FAB M0 or M3 AML need to be conducted to clarify the prognostic significance of CD34.

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REFERENCES

1. Fruchart C, Lenormand B, Bastard C, Boulet D, Lesesve JF, Callat MP, Stamatoullas A, Monconduit M, Tilly H: Correlation between CD34 expression and chromosomal abnormalities but not clinical outcome in acute myeloid leukemia. Am J Hematol 53:175–180, 1996.
2. Guinot M, Sanz GF, Sempere A, Arilla MJ, Jarque I, Gomis F, Sanz MA: Prognostic value of CD34 expression in de novo acute myeloblastic leukemia. Br J Haematol 79:533–534, 1991.
3. Myint H, Lucie NP: The prognostic significance of the CD34 antigen in acute myeloid leukemia. Leuk Lymph 7:425–429, 1992.
4. Fagioli F, Cuneo A, Carli MG, Bardi A, Piva N, Previati R, Rigolin GM, Ferrari L, Spanedda R, Castoldi G: Chromosome aberrations in CD34-positive acute myeloid leukemia. Cancer Genet Cytogenet 71:119–124, 1993.
5. Ciolli S, Leoni F, Caporale R, Pascarella A, Salti F, Rossi Ferrini P: CD34 expression fails to predict the outcome in adult acute myeloid leukemia. Haematologica 78:151–155, 1993.

Complete Remission of a Primary Effusion Lymphoma With Antiretroviral Therapy

To the Editor: Primary effusion lymphoma (PEL) is an uncommon subset of AIDS-related lymphomas that grow mainly in the body cavities. This distinct clinicopathologic entity is associated with the Kaposi's sarcoma-associated herpes virus (KSHV/HHV-8) [1]. Regression of Kaposi's sarcoma lesions [2] and decrease in HHV-8 plasma viral load [3] have recently been reported in HIV-infected patients receiving a protease inhibitor. We report on a patient with PEL who achieved a persistent complete remission after the initiation of antiretroviral therapy.

In January 1996, a 66-year-old white homosexual man was referred because of fever, weight loss and chest pain. Physical examination and chest X-ray revealed left unilateral pleural effusion. There was no lymphadenopathy, no splenomegaly, and no Kaposi's sarcoma. Extensive oral hairy leukoplakia (OHL) was present. A serological test for HIV was positive. The CD4+ and CD8+ cell counts were 33×10^6/L (3%) and 913×10^6/L (83%), respectively. Plasma HIV RNA level was 36,900 copies/mL (Amplicor HIV-1 Monitor, Neuilly s/seine Roche). Cytological examination and immunophenotypic analysis of the pleural fluid disclosed the presence of large immunoblastic and anaplastic CD19− CD3− tumor cells, mixed with normal CD3+ CD8+ CD45RO+ cells. Southern blot analysis for immunoglobulin gene rearrangement and specific viral DNA sequences (EBV, HHV-8) showed that the malignant cells were clonal B cells and were positive for the presence of both EBV and HHV-8. A CT scan of the thorax and abdomen was normal excepted for the presence of a pleural effusion. A bone marrow biopsy was normal. The patient was started with zidovudine and zalcitabine therapy. At week 10, a complete remission was achieved for both PEL and OHL. The CD4+ cell count was 214×10^6/L (8%) and the plasma HIV RNA level was 2,200 copies/mL; at week 36, the CD4+ cell count was 164×10^6/L (14%) and the plasma HIV RNA level was <200 copies/mL. In April 1997, after a 16-month follow-up, there was no evidence of PEL relapse and the patient remains asymptomatic.

HHV8, a new herpesvirus, is closely associated in HIV-infected patients, with three proliferative disorders: Kaposi's sarcoma [4], primary effusion lymphoma [1], and Castleman's disease [5]. However, the direct transforming capacity of this virus remains under discussion. Dysregulated production of cytokines (bFGF, IL6, IL10) as well as some HIV gene products (TAT) may play a key role in the initiation of the lesion. In the case of PEL, most of the tumors are infected with both HHV-8 and EBV, suggesting a potential synergistic interaction of these viruses in the pathogenesis of the disease. In the present case, there was a concomitant regression of PEL and OHL. The important reduction in HIV viral load (>2 logs) and the increase in CD4+ lymphocyte count under antiretroviral therapy was associated with a prolonged remission of PEL. Since it is unlikely that anti-HIV drugs had a direct effect on EBV and/or HHV-8, the benefit of this therapy on both PEL and OHL rather suggests an indirect effect on the production of HIV proteins and cellular cytokines as well as on immune reconstitution.

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REFERENCES

1. Cesarman E, Chang Y, Moore PS, Said JW, Knowles DM: Kaposi's sarcoma-associated herpesvirus-like DNA sequences in AIDS-related body-cavity-based lymphomas. N Engl J Med 332:1186–1191, 1995.
2. Murphy M, Armstrong D, Sepkowitz KA, Myskowski PL: Regression of AIDS-related Kaposi's sarcoma following treatment with an HIV-1 protease inhibitor. AIDS 11:261–262, 1997.
3. Rizzieri DA, Liu J, Traweek ST, Miralles GD: Clearance of HHV-8 from peripheral blood mononuclear cells with a protease inhibitor. Lancet 349:775–776, 1997.
4. Chang Y, Cesarman E, Pessins MS, Lee F, Culpepper J, Knowles DM, Moore PS: Identification of herpes-like DNA sequences in AIDS-associated Kaposi's sarcoma. Science 266:1865–1869, 1994.
5. Soulier J, Grollet L, Oksenhendler E, Cacoub P, Cazals-Hatem D, Babinet P, D'Agay MF, Clauvel JP, Raphael M, Degos L, Sigaux F: Kaposi's sarcoma-associated herpes-like DNA sequences in multicentric Castleman's disease. Blood 84:1278–1280, 1995.

Spontaneous Splenic Rupture as the Initial Presentation of Plasma Cell Leukemia: A Case Report

To the Editor: Plasma cell leukemia (PCL) is an infrequently encountered type of plasma cell dyscrasias. It may be either primary or secondary as a result of transformation of multiple myeloma (MM). It has an extremely

aggressive clinical course and the mean life expectancy is 3 months after diagnosis. The diagnosis of PCL depends upon the appearance of more than 20% plasma cells in the peripheral smear and absolute plasma cell content of a minimum of 2×10^9/L in association with a neoplastic plasma cell proliferation [1–3]. We report a case of aggressive PCL, which presented with spontaneous splenic rupture, hemorrhagic shock, and multiorgan failure. The patient was a 40-year-old man and had undergone a laparoscopic cholecystectomy 5 months before. A complete blood, urinalysis, and routine biochemistry were unremarkable at that time. He had a history of mild left upper abdominal pain, fatigue, and had been experiencing night sweats for 3 weeks. He denied any abdominal trauma. He presented with profound shock, abdominal pain, and distention. His hemoglobin was 9.6 g/dl, Hct% 26, WBC: 24.2×10^9/L, platelet count 133×10^9/L, erythroid sedimentation rate 81 mm/1 hr, BUN 32 mg/dl, creatinine 2 mg/dl, serum total calcium 10.5 mg/dl. His prothrombin time was 18 sec (with a control of 12 sec and an INR of 2 sec), activated partial thromboplastin time of 51 sec (normal limits 35–45 sec), and a bleeding time 8 min. Ultrasound examination revealed massive fluid accumulation in the abdomen and an emergency laparotomy revealed a ruptured spleen and an intraabdominal hemorrhage. A splenectomy was performed and the patient was admitted to the intensive care unit with multiorgan failure, which required hemodialysis and mechanical ventilation. His peripheral smear showed plasma cells constituting 30% of the differential count. Pathological examination of the spleen and a bone marrow biopsy disclosed diffuse infiltration with pleomorphic, primitive cells. Serum immunoelectrophoresis showed a monoclonal IgG kappa spike. Flow cytometric immunophenotyping revealed the following phenotype: CD 10^-, 13^-, 19^-, 20^-, 33^-, 38^+, 56^+, HLA DR^+, Tdt^-. He developed three additional major intraabdominal bleeding episodes, which required revision and fresh frozen plasma and platelet transfusions. Despite supportive treatment and chemotherapy with prednisolone and melphalan, he died 2 weeks after the initial presentation.

As previously described, in contrast to PCL secondary to MM, primary PCL has a very short duration of presenting symptoms and a notorious clinical course [1–3]. It is usually resistant to chemotherapy. The 5-year relative survival rate has been reported as 13% [4]. Lytic bone lesions, bone pain, hypercalcemia, and prominent M protein secretion are infrequent in primary PCL [1–3]. On the other hand, organomegaly and bleeding are common in PCL [5]. A complete blood count and full-biochemistry screening and normal hemostasis after a major surgical intervention 5 months earlier, excludes the possibility of an underlying myeloma and confirms the very rapid onset of primary PCL. Although he had mild hypercalcemia (10.8–11.2 g/dl) and prominent M protein secretion, lytic bone lesions were undetectable. The acute renal failure is due to the combined effects of acute hemorrhagic shock and toxic effects of light chain excretion. To our knowledge, this is the first case of PCL presenting with spontaneous splenic rupture.

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References

1. Kyle RA, Maldonado JE, Bayrd ED, Rochester M: Plasma cell leukemia. Reports on 17 cases. Arch Int Med 133:813, 1974.
2. Kosmo MA, Gale RP: Plasma cell leukemia. Semin Hematol 24:202, 1987.
3. Woodruff RK, Malpas JS, Paxton AM, Lister TA: Plasma cell leukemia: A report on 15 patients. Blood 52:839, 1978.
4. Hernandez JA, Land KJ, McKenna-RW: Leukemias, myeloma, and other lymphoreticular neoplasms. Cancer 75(suppl 1):381, 1995.
5. Glaspy JA: Hemostatic abnormalities in multiple myeloma and related disorders. Hematol/Oncol North Am 6:1301, 1992.